Appl. No. 10/052,589

Amdt. dated: November 9, 2004

Reply to Office Action of May 19, 2004

Amendments to the Specification:

Please amend the figure description beginning on page 3, line 19 as follows:

Figure 2 is the DNA sequence, SEQ ID NO. 3, of the promoter of the murine α_{1B} adrenergic receptor.

Please amend the figure description beginning on line 22 of page 3, as follows:

Figure 4. (A) A map of the transgene construct showing the size of EcoRI fragments and the binding sites for α_{1B} - and SV40-specific southern probes. Three different transgenes were constructed with the only difference between each being the $\alpha_{1B}AR$ cDNA used (either the wildtype (WT), single mutant or triple mutant cDNA). Transgenic animals whose genome contain the wild-type transgene are designated W; transgenic animals whose genome contain the single mutant transgene are designated S; and transgenic animals whose genome contain the triple mutant transgene are designated T. Each founder transgenic animal and its progeny are also given a numerical designation. For example, one of the founder transgenic animals whose genome contains the wild-type transgene, and its progeny, is referred to as "W1", while another transgenic founder animal whose genome contains the wild-type transgene, and its progeny, is referred to as "W2". (B) Southern blot analysis of genomic DNA from nontransgenic (NT)(-/-), heterozygous (+/-) and homozygous (+/+) W2 mice. Tail DNA samples were digested with EcoRI, run on 0.8% agarose gels, transferred to nitrocellulose and probed with either the α_{1B} probe or the SV40 probe. The α_{1B} probe hybridized to 3.0 and 1.6 kb fragments which represented the endogenous α_{1B}AR gene and the transgene respectively. Comparatively, the SV40 probe hybridized only to a 1.4 kb fragment which represented the transgene. (C) B_{max} determination was carried out via saturation binding in various α_{1B}AR -positive and -negative tissues using the α_1 -antagonist 2- $[\beta$ -(4-hydroxyl-3- $[^{125}I]$ iodophenyl)ethylaminomethyl]tetralone ($[^{125}I]HEAT$) as the radioligand. B_{max} values in W2+/- mice that were significantly different from the corresponding non-transgenic (NT) values are labeled with an asterisk. Error bars represent SEM (N>5 for each tissue) and significance was determined using analysis of variance with a two-tailed Student's t test (p<0.05). (D) Inositol tri-phosphate (IP₃)levels. Error bars represent SEM (n=3 for each line) and significance was determined using analysis of variance with a two-tailed Student's t test (p<0.05). The asterisk (*) indicates significance from the NT Appl. No. 10/052,589

Amdt. dated: November 9, 2004

Reply to Office Action of May 19, 2004

group. The dagger (†) indicates significant increases compared to the W2+/- group. The double cross (‡) indicates significant increases compared to the S l+/- group. (E) Hybridization pattern of the SV40 probe in a section cut from a NT mouse. (F) Hybridization pattern of the α_{1B} probe to endogenously expressed $\alpha_{1B}AR$ transcripts in a NT brain section. (G) Hybridization of the SV40 probe to message transcribed from the transgene in the brain of a W2+/- mouse. Cx = cortex; Rt = reticular thalamic nuclei; Hy = hypothalamus. (H) Transgene expression detected by the alB probe. These positive regions coincide with regions identified in C and overlap the background expression of the endogenous gene.